

Preferentially Cytotoxic to Leukemia and Selected Solid Tumor Cells.

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JOURNAL: Blood 100 (11): pAbstract No. 4411 November 16, 2002 2002

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SPONSOR: American Society of Hematology

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RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: Selenium (Se) is an essential trace mineral. Dietary Se deficiency has been linked to Keshan Disease and an increased incidence of cancer and cardiovascular disease. Se compounds have been used in preclinical models and, to a limited extent in the clinic, for the treatment of cancer. All biological activities of Se have been attributed to ionized or organic Se, i.e. Se in oxidation states -II, +II, +IV, or +VI. Elemental Se (Se in oxidation state 0) has been considered biologically inert. We report here that Se(0) generated by the singlet oxygen-mediated photobleaching of selenomercocyanine photosensitizers combines with certain serum macromolecules (notably albumin and lipoproteins) to form conjugates that are selectively cytotoxic for leukemia and selected solid tumor cells. For example, a 1-hour exposure to an 8- μ M solution of Se-conjugates is sufficient to eliminate 5 log of in vitro clonogenic L1210/L-PAM2 leukemia cells while preserving all normal granulocyte/macrophage progenitors and CD34-positive cells. In some preclinical models, Se-conjugates synergistically potentiate the anti-tumor effect of ionizing radiation and alkylating agents. In order to express their cytotoxic potential, Se-conjugates need to be internalized by a non-lysosomal process that is inhibited by low temperature, cytochalasin B, and excess native carrier protein. However, the protein and lipoprotein content of whole blood is not sufficient to block the selective uptake of conjugates by leukemia cells. Internalization of Se-conjugates is followed by a rapid and massive (up to 80%) drop of intracellular glutathione, a loss of mitochondrial transmembrane potential, and the activation of caspases. Se conjugates that are derived from mercocyanines with a S or Se atom in the donor heterocycle are green-fluorescent due to the binding of a chromophore photoproduct to the carrier molecule. The fluorescent label allows easy analysis of the binding/uptake and distribution of Se-conjugates by flow cytometry. Our results demonstrate that photoproducts can contribute substantially to the cytotoxic action of photodynamic therapy. They offer a plausible explanation for the reduced cytotoxic activity of selenone photosensitizers at low temperatures, and they question the widely held view that Se (0) is inert. Compounds modeled after our Se-conjugates may prove useful for the local or systemic therapy of cancer.

REGISTRY NUMBERS: 14930-87-6: caspase; 14930-96-2: cytochalasin B; 70-18-8: glutathione; 7782-49-2: selenium

ENZYME COMMISSION NUMBER: 3.4.22.36: caspase

DESCRIPTORS:

MAJOR CONCEPTS: Toxicology

BIOSYSTEMATIC NAME: Infusoria: Animalia

BEST AVAILABLE COPY

ORGANISMS: animal (Mammalia)
 ORGANISMS: PARTS AND SUBPARTS--blood and lymphatics
 COMMON TAXONOMIC TERMS: animals
 DISEASES: cancer--neoplastic disease, therapy; leukemia--blood and lymphatic disease, neoplastic disease
 MESH TERMS: Neoplasms (MeSH); Leukemia (MeSH)
 CHEMICALS & BIOCHEMICALS: caspase--regulation; cytochalasin B; glutathione; selenium--generation
 METHODS & EQUIPMENT: photodynamic therapy--clinical techniques, therapeutic and prophylactic techniques
 MISCELLANEOUS TERMS: mitochondrial transmembrane potential; Meeting Abstract; Meeting Poster

CONCEPT CODES:

00520 General biology - Symposia, transactions and proceedings
 10064 Biochemistry studies - Proteins, peptides and amino acids
 10069 Biochemistry studies - Minerals
 10802 Enzymes - General and comparative studies: coenzymes
 12512 Pathology - General
 15002 Blood - Blood and lymph studies
 15004 Blood - Blood cell studies
 15006 Blood - Blood, lymphatic and reticuloendothelial pathologies
 24004 Neoplasms - Pathology, clinical aspects and systemic effects
 24008 Neoplasms - Therapeutic agents and therapy
 24010 Neoplasms - Blood and reticuloendothelial neoplasms

BIOSYSTEMATIC COLLECT:

33000 Animalia

1/9/2 (Item 2 from file: 5)
 DIALOG(R) File: BICISIS: Reviews(R)
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0012546247 BIOSIS ID: 10000204500

Albumin uptake defines sensitivity to selenomercocyanine -derived photoproduct-albumin adducts

AUTHOR: Tsujino I, Iwano (Reprint); Bousbaa J; Sieber F (Reprint)

AUTHOR ADDRESS: Mail Box 1 of Wisconsin, Milwaukee, WI, USA**USA

JOURNAL: Proceedings of the American Association for Cancer Research Annual Meeting (41): p700 March, 2000 2000

MEDIUM: print

CONFERENCE/MEETING: 91st Annual Meeting of the American Association for Cancer Research. San Francisco, California, USA April 01-05, 2000;

20000401

ISSN: 0197-016X

DOCUMENT TYPE: Meeting; Meeting Poster

RECORD TYPE: Citation

LANGUAGE: English

REGISTRY NUMBERS: 14-30-96-2: cytochalasin B; 70-18-8: glutathione

DESCRIPTORS:

MAJOR CONCEPTS: Photochemistry and Molecular Biophysics; Pharmacology; Tumor Biology

BIOSYSTEMATIC TERMS: Humans--Primates, Mammalia, Vertebrata, Chordata, Animalia; Humans--Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGANISMS: H69 cell line (Hominidae)--human small cell lung cancer cells; L1210 cell line (Muridae)--murine leukemia cells

COMMON TAXONOMIC TERMS: Humans; Primates; Animals; Chordates; Mammals; Nonhuman Vertebrates; Nonhuman Mammals; Rodents; Vertebrates

CHEMICALS & BIOCHEMICALS: albumin--uptake; cytochalasin B; glutathione--intracellular; photoproduct-albumin adducts--antineoplastic activity,

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selenomerocyanine -derived

MISCELLANEOUS ITEMS: Meeting Poster; Meeting Poster

CONCEPT CODES:

24002 Neoplasms - General
02506 Cytology - Animal
10060 Biochemistry - General
10502 Biophysics - General
16001 Respiratory system - General and methods
22002 Pharmacology - General
15001 Blood - General and methods
00520 General biology - Symposia, transactions and proceedings

BIOSYSTEMATIC CODES:

86215 Hominidae
86375 Muridae

1/9/3 (Item 1 from file: 34)

DIALOG(R) File 34: Selenomerocyanine (R) Cited Ref Sci

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11737957 Genuine Item Number: 61432 Number of References: 0

Title: Colloidal selenium generated by photobleaching of selenomerocyanine dyes combines with serum macromolecules to form conjugates that are preferentially cytotoxic to leukemia and selected solid tumor cells

Author(s): Sieben P; Lazzaro JP; Anderson GS; Miyagi K; Sampson RW; Tsujino L; Gunther WB; Kriegl M; Bousbaa J; Forsterling FH

Corporate Source: Med Coll Wisconsin, Milwaukee//WI/53226; WHHG Consulting, W Chester//PA; Univ Wisconsin, Milwaukee//WI/53201

Journal: BLOOD, 2002, V100, N11,2 (NOV 16), P224B-224B

ISSN: 0006-4971 Publication date: 20021116

Publisher: AMER SOC HEMATOLOGY, 1900 M STREET, NW SUITE 200, WASHINGTON, DC 20036 USA

Language: English Document Type: MEETING ABSTRACT

Meeting Abstract Number: 4111

Geographic Location: US

Journal Subject Category: HEMATOLOGY

? s selenomerocyanine

SC 0 0 000X 0L

? logoff y

C2mar05 11:41:00 User: 276653 Session D24.2

\$0.26 \$0.044 DialUnits File5

\$4.00 2 Type(s) in Format 9

\$4.00 2 Types

\$4.26 Estimated Cost File5

\$0.51 \$0.027 DialUnits File34

\$0.43 1 Type(s) in Format 9

\$6.43 1 Type

\$7.02 Estimated Cost File34

\$0.07 \$0.011 DialUnits File35

\$0.07 Estimated Cost File35

\$0.19 \$0.021 DialUnits File40

\$0.19 Estimated Cost File40

\$0.07 \$0.018 DialUnits File50

\$0.03 Estimated Cost File50

\$0.11 \$0.027 DialUnits File65

\$0.10 Estimated Cost File65

\$0.07 \$0.009 DialUnits File71

\$0.07 Estimated Cost File71

\$0.12 \$0.027 DialUnits File73

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\$0.28 Estimated cost File73
 \$0.08 0.018 DialUnits File91
 \$0.08 Estimated cost File91
 \$0.02 0.017 DialUnits File94
 \$0.09 Estimated cost File94
 \$0.02 0.001 DialUnits File98
 \$0.02 Estimated cost File98
 \$0.15 0.027 DialUnits File110
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 \$0.59 Estimated cost File434
 \$0.06 0.001 DialUnits File467
 \$0.06 Estimated cost File467
 One search, 25 DialUnits, 0.569 DialUnits FileOS
 \$0.80 TERMINATE
 \$15.44 Estimated cost of this search
 \$15.55 Estimated total session cost 0.777 DialUnits

Logoff: level 05.00.10 00:00:00

You are now logged off

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Trying 31060000009999...Open

DIALOG INFORMATION SERVICES

PLEASE LOGON:

***** HHHHHHHH SSSSSSSS? ### Status: Signing onto Dialog *****

ENTER PASSWORD:

***** HHHHHHHH SSSSSSSS? *****

Welcome to DIALOG

Status: Login successfulDialog level 05.00.10aD

Last logoff: 01mar05 11:25:06

Logon file405 09mar05 10:55:29

*** ANNOUNCEMENT ***

--Important Notice to Freelance Authors--

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NEW FILES RELEASED

***FDAnews (File 182)

***German Patents Fulltext (File 324)

***Beilstein Abstracts (File 393)

***Beilstein Facts (File 390)

***Beilstein Reactions (File 391)

RELOADED

***Medline (Files 154 & 155)

RESUMED UPDATING

***Canadian Business and Current Affairs (262)

>>> Enter BEGIN HOMEBASE for Dialog Announcements <<<

>>> of new databases, price changes, etc. <<<

* * *

SYSTEM:HOME

Cost is in DialUnits

Menu System II: D2 version 1.7.9 term=ASCII

*** DIALOG HOMEBASE(SM) Main Menu ***

Information:

1. Announcements (new files, reloads, etc.)
2. Database, Rates, & Command Descriptions
3. Help in Choosing Databases for Your Topic
4. Customer Services (telephone assistance, training, seminars, etc.)
5. Product Descriptions

Connections:

6. DIALOG(R) Document Delivery
7. Data Star(R)

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/H = Help

/L = Logoff

/NOMENU = Command Mode

Enter an option number to view information or to connect to an online service. Enter a BEGIN command plus a file number to search a database (e.g., B1 for ERIC).

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Terminal set to DLINK

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Information:

1. Announcements (new files, reloads, etc.)
2. Database, Rates, & Command Descriptions
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/NOMENU = Command Mode

Enter an option number to view information or to connect to an online service. Enter a BEGIN command plus a file number to search a database (e.g., B1 for ERIC).

? LOGOFF

09mar05 10:56:17 User276653 Session D23.1
\$0.00 0.213 DialUnits FileHomeBase
\$0.00 Estimated cost FileHomeBase
\$0.21 TELNET
\$0.21 Estimated cost this search
\$0.21 Estimated total session cost 0.213 DialUnits

Logoff: level 05.00.10a D 10:56:17

You are now logged offTrying 31060000009999...Open

DIALOG INFORMATION SERVICES

PLEASE LOGON:

***** HHHHHHHH SSSSSSS? ### Status: Signing onto Dialog *****

ENTER PASSWORD:

***** HHHHHHHH SSSSSSS? *****

Status: Login successfulWelcome to DIALOG

Dialog level 05.00.10aD

Last logoff: 09mar05 10:56:17

Logon file405 09mar05 11:04:35

* * *

SYSTEM:HOME

Cost is in DialUnits

Menu System II: D2 version 1.7.9 term=ASCII

*** DIALOG HOMEBASE(SM) Main Menu ***

Information:

1. Announcements (new files, reloads, etc.)
2. Database, Rates, & Command Descriptions
3. Help in Choosing Databases for Your Topic
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Enter an option number to view information or to connect to an online service. Enter a BEGIN command plus a file number to search a database (e.g., B1 for ERIC).

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*** DIALOG HOMEBASE(SM) Main Menu ***

Information:

1. Announcements (new files, reloads, etc.)
2. Database, Rates, & Command Descriptions
3. Help in Choosing Databases for Your Topic
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/NOMENU = Command Mode

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? b biosci

```
09mar05 11:05:03 User276653 Session D24.1
$0.00      0.207 DialUnits FileHomeBase
$0.00 Estimated cost FileHomeBase
$0.11 TELNET
$0.11 Estimated cost this search
$0.11 Estimated total session cost 0.207 DialUnits
```

SYSTEM:OS - DIALOG OneSearch

- File 5:Biosis Previews(R) 1969-2005/Feb W4
(c) 2005 BIOSIS
- File 34:SciSearch(R) Cited Ref Sci 1990-2005/Feb W4
(c) 2005 Inst for Sci Info
- File 35:Dissertation Abs Online 1861-2005/Feb
(c) 2005 ProQuest Info&Learning
- File 40:Enviroline(R) 1975-2005/Feb
- File 50:CAB Abstracts 1972-2005/Feb
(c) 2005 CAB International
- File 65:Inside Conferences 1993-2005/Mar W1
(c) 2005 BLDSC all rts. reserv.
- File 71:ELSEVIER BIOBASE 1994-2005/Feb W4

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File 73:EMBASE 1974-2005/Feb W4
(c) 2005 Elsevier Science B.V.
File 91:MANTIS(TM) 1880-2005/Feb
2001 (c) Action Potential
File 94:JICST-EPlus 1985-2005/Jan W4
(c) 2005 Japan Science and Tech Corp (JST)
File 98:General Sci Abs/Full-Text 1984-2004/Dec
(c) 2005 The HW Wilson Co.
File 110:WasteInfo 1974-2002/Jul
(c) 2002 AEA Techn Env.
***File 110: This file is closed (no updates)**
File 135:NewsRx Weekly Reports 1995-2005/Feb W4
(c) 2005 NewsRx
***File 135: New newsletters are now added. See Help News135 for the complete list of newsletters.**
File 143:Biol. & Agric. Index 1983-2005/Jan
(c) 2005 The HW Wilson Co
File 144:Pascal 1973-2005/Feb W4
(c) 2005 INIST/CNRS
File 155:MEDLINE(R) 1951-2005/Mar W1
(c) format only 2005 The Dialog Corp.
***File 155: Medline has been reloaded; accession numbers have changed.**
Please see HELP NEWS 154.
File 164:Allied & Complementary Medicine 1984-2005/Mar
(c) 2005 BIOSIS
File 172:EMBASE Alert 2005/Feb W4
(c) 2005 Elsevier Science B.V.
File 185:Zoological Record Online(R) 1978-2005/Mar
(c) 2005 BIOSIS
File 357:Derwent Biotech Res. 1982-2005/Mar W2
(c) 2005 Thomson Derwent & ISI
File 369:New Scientist 1994-2005/Feb W3
(c) 2005 Reed Business Information Ltd.
File 370:Science 1996-1999/Jul W3
(c) 1999 AIMS
***File 370: This file is closed (no updates). Use File 47 for more current information.**
File 391:Beilstein Extractions Nov. 2004
(c) 2005 Beilstein GmbH
File 434:SciSearch Cited Ref Sci 1974-1989/Dec
(c) 1998 Inst for Sci Info
File 467:ExtraMED(tm) 2000/Dec
(c) 2001 Informania Ltd.
***File 467: F467 no longer updates; see Help News467.**

7.

```

Set  Items  Description
---  ---
? s selenomercyanine
   S1      3  Selenomercyanine
? t s1/9/all

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1/9/1 (Item 1 from file: 5)
DIALOG(R)File 5:File's Preview(R)
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0014409176 BIOSIS MFI: 200300367895

**Colloidal Selenium Generated by Photobleaching of Selenomercyanine Dyes
Combines with Serum Proteins To Form Conjugates That Are**